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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,981	01/25/2001	Aladar A. Szalay	13070-1	5416

7590 03/22/2005

SHELDON & MAK
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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/769,981	SZALAY ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *23-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 26, 2005 has been entered.

Election/Restrictions

2. Applicants' traverse the withdrawal of claims 23-32 and the election of claims 1-12 even though applicant received actions on the merits for the originally presented invention of claims 1-12 on March 3, 2003, August 7, 2003 and August 27, 2004.

The traversal is on the ground(s) that claim 23 mirrors claim 10. This is not found persuasive because the method described in claims 23-32 is patentably distinct. The methods are distinct as claimed because claims 23-32 have different method steps, with different functions and those effects result in different final outcomes. Claims 23-32 are drawn to a method for evaluating whether a material will allow bacteria to pass through, around or into the material using a distinctly different modified bacteria, i.e., a bacteria that comprises two separately detectable signals. Moreover, claims 23-32 are further drawn to an evaluation method wherein the method places the modified bacteria in the center of a hollowed out, extracted natural tooth where the root end of the tooth is

sealed with the material, thus this method has a different function. The method of claim 1 is not drawn to an evaluation method wherein the method places the modified bacteria in the center of a hollowed out, extracted natural tooth where the root end of the tooth is sealed with the material, thus this method has a different function. Furthermore, the method of claims 23-32 does not produce the same results. The groups produce different effects and different functions when compared to the other group. Therefore, the inventions are unrelated. The requirement is still deemed proper and is therefore made FINAL.

It is noted that the invention of claims 1-12 has been constructively elected by original presentation for prosecution on the merits. Moreover, applicants originally elected without traverse, thereby waiving their traversal rights. Accordingly, claims 23-32 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Therefore, claims 1-12 are under consideration in this office action.

Amendment Entry

4. The amendment filed January 21, 2005 has been entered. Claims 1-3, and 9-10 have been amended. Claims 13-22 have been cancelled. Claims 23-32 are withdrawn. Claims 1-12 are under consideration in this office action.

Withdrawal of Rejections

5. The rejection of claims 1-8 and 11 under 35 U.S.C. 103(a) as being unpatentable over Miller et al., (US Patent 5,736,351) in view of Contag et al., is withdrawn in view of applicants amendments and arguments.

Response to Arguments

6. Applicant's arguments filed January 21, 2005 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The rejection of claims 1-2, 4, 7 and 11 under 35 U.S.C. 102(b) as being anticipated by Loessner et al., is maintained for reasons already of record. The rejection was on the grounds that Loessner et al., teach a method for evaluating whether an implantable material will allow modified living bacteria to pass through the implantable material or around the implantable material or into the implantable material comprising providing living bacteria with a first detectable signal; placing the modified bacteria on the first side of the implantable material and detecting whether the first signal is present on the implantable material.

Applicants' assert that Loessner et al., do not teach living bacteria which are modified to produce a first detectable signal, also referred to by the instant claims as modified living bacteria. However the claims do not limit how the living bacteria are modified to produce a detectable signal. Rather the claims simply require that the living bacteria be somehow modified to produce a detectable signal. The bacteria of Loessner et al., is living. The authors created a modified luciferase gene that was introduced into the bacterial *Listeria* host. The introduction of the luciferase gene into the bacteria did not kill the bacteria, rather the living bacteria of Loessner et al., is now modified in such a way as to produce detectable signal. Furthermore, Loessner et al, states that the luciferase expression mediated is strictly dependant on the presence of *Listeria* cells which must be viable. Heat inactivated cells yield no signal (page 2964). Thus Loessner et al., clear teach providing living bacteria which are modified to produce a first detectable signal. Therefore applicants' arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The rejection of claims 9-10 and 12 under 35 U.S.C. 103(a) as being unpatentable over Miller et al., (US Patent 5,736,351) and Contag et al., and further in

view of Holen (US Patent 5,814,331) is maintained. The rejection was on the grounds that it would have been prima facie obvious at the time of applicants' invention to modify the methods taught by Miller et al., and Contag et al., to detect bacterial contamination on teeth as taught by Holen. Miller et al., and Contag et al., have been discussed above.

Applicants' assert that in view of the arguments drawn to Miller et al., and Contag et al, this rejection should be withdrawn. However, it is the examiner's position that the rejection should be maintained, contrary to applicants' assertion. In this case, one would have a reasonable expectation of success because no more than routine skill would have been required to exchange the materials of Miller et al., and Contag et al., for a tooth, since the art teaches that bacterial contamination of teeth can cause periodontal diseases. Moreover, no more than routine skill would have been required to exchange the material being tested because it was already known in the art to be able to detect the bacteria on tooth surfaces. Thus, applicants' assertions are not persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-8, 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al., (US Patent 5,736,351) in view of Billiard et al.

The claims are drawn to a method for evaluating whether an implantable material will allow modified living bacteria to pass through the implantable material or around the implantable material or into the implantable material comprising: a) providing modified bacteria to produce a first detectable signal; b) placing the modified bacteria on the first side of the implantable material; and c) detecting whether the first signal is present on the implantable material where the implantable material is non-living. The dependant claims are drawn to the signal being in the visible spectrum and the bacteria incorporating functional luciferase and a second green fluorescent protein detectable signal.

Miller et al., teach methods for rapidly determining the presence and quantity of specific microbial or chemical contaminant present on a wide variety of surfaces, including surfaces of meat carcasses, liquid samples, medical and food service equipment, gloves, and material in medical situations (col. 1 lines 10-22). Thus Miller et al., teach a method for the determining bacterial contamination on any type of non-living material, just as instantly claimed. It is noted that implantable material is simply defined by the instant specification as any material useable for implantation. Thus, Miller et al., teaching of detecting contamination on a wide variety of surfaces that includes but is not limited to meat carcasses, which is non-living material and materials used in medical situations such as wound closure material which is encompassed by the broad definition of implantable material. The invention determines contamination by bioluminescent or

chemiluminescent techniques (col. 1 lines 22-25). Luminescent reactions and test procedures using bioluminescent reactions for bacterial determination are well known in the art (col. 2 lines 15-55). Miller et al., teach well-known culturing techniques drawn to selective growth and antibiotic resistance features. The invention teaches using live bacteria in a sample and adding a bacterial lysing agent that allows for the release of microbial ATP, adding ATP free luciferin and luciferase and determining the amount of light emitted from the interaction. Thus the inventors teach providing living bacteria that were modified by the lyses step, to produce a first detectable signal that was exposed to sample material as required by the claims. Another embodiment teaches providing living *Salmonella* bacteria are modified by a horseradish peroxidase labeled antibody directed against the bacteria. (col. 13 lines 1-8). Thus the living bacterium is modified to produce a first detectable signal as required by the claims. It is noted that the specification at page 5 defines modified to mean that the modified bacteria produce a detectable signal. Example 2 teaches a general screen on carcasses wherein the modified bacteria are exposed to the implantable material. Example 3 teaches placing the modified bacteria onto the disposable test device followed by detecting the bioluminescent signal on the test device using a luminometer. Thus Miller et al., has exposed the modified bacteria to the material being tested. Table 2 shows results displaying the detection of bioluminescent signal. Thus Miller et al., teach determining whether signal is present on the material. However Miller et al., do not teach using bacteria that are modified to incorporate a functional green fluorescent protein or luciferase protein.

Billard et al., teach bioluminescence-based assays for the detection and characterization of bacteria in clinical laboratories. This phenomenon, known as bioluminescence, can be used to detect a cell's presence and physiological status (page 2). Moreover, when coupled to the expression of individual genes, the light producing enzymes can serve as a "reporter assay" via gene expression in cells (page 2). Examples of these enzymes include the luciferase enzymes from bacteria (*lux*) and eukaryotes (*luc*). The genes encoding luciferase was introduced into the genome of a bacterial virus (bacteriophage) and then the recombinant bacteriophage infects a host bacterium that provides for light production. Thus, Billard et al., teach a living modified host bacterium which has incorporated functional luciferase protein, just as required by the claims. Another bioluminescent protein is green fluorescent protein (GFP), which is characterization by the *gfp* gene and is expressible in prokaryotic and eukaryotic systems. Therefore this reporter gene can be expressed and localized in living cells. Thus, Billard et al., teach a living modified host bacterium which has incorporated functional green fluorescent protein, just as instantly claimed. Moreover, the bacterium is administrable to an animal or human just as claimed. The major advantage it provides compared to other reporters is that GFP fluorescence does not require the addition of exogenous substrate or cofactors and can be generated simply by excitation with long UV wavelengths. Moreover, other versions of GFP have been described, including a mutant that produces blue fluorescence and red-shifted excitation mutants. Thus, the signals produced light emissions in the visible spectrum, just as required by the claims.

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the methods of Miller et al., to detect bacterial contamination using bacteria that produces a detectable signal and incorporate a modified bacterium that expresses GFP and/or luciferase to produce a detectable signal to as taught by Billard et al., in the method of evaluation. One would have a reasonable expectation of success because no more than routine skill would have been required to exchange the modified bacteria of for the well-known modified bacteria of Billard et al., which was also known in the art to be useable to detect bacterial contamination. No more than routine skill would have been required to make the modified bacteria that was already known in the art to be able to detect the bacteria. Moreover, no more that routine skill is required to use a well-known alternative and functionally equivalent luminescent reporter in a modified bacterium that is known in the art to be useful for the purpose of signal detection. And there would have been a reasonable expectation of success by one skilled in the art since GFP and luciferase expression techniques are well known in the art to be rapid, not require exogenous reagents and convenient when compared to other detection methods.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-8 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 10/356,245. Although the conflicting claims are not identical, they are not patentably distinct from each other because even through the preamble of the claims of 10/356,245 is drawn to a method for the evaluation of a material to determine whether the material is susceptible to bacterial contamination or colonization when implanted into an animal or human comprising: a) providing modified bacteria to produce a first detectable signal; b) exposing the material to the modified bacteria; and c) determining whether the modified bacteria is present on the material, the steps within the method recite the same steps as the claims in instant application 09/769,981. The claims of 09/769,981 are drawn to a method for evaluating whether a material will allow modified living bacteria to pass through the material or around the material or into the material comprising: a) providing living modified bacteria to produce a first detectable signal; b) a placing the modified bacteria on the material; and c) a detecting whether the signal is present on the material or within the material. Both methods provide the modified bacteria, allow for contacting the bacteria with the material and determine or detect whether the modified bacteria is present on the material based on the first detectable signal.

Thus, the method steps are not patentably distinct. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
March 15, 2004

L. F. Smith
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